Applicants have repeated the amendments requested in the Preliminary Amendment with reference to the paragraph numbers included in the substitute specification. Applicants respectfully request the entry of these amendments.

The Claims Are Supported by the Specification

The Examiner rejected claim 26 as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. *Id.*, page 3. The Examiner states that, except for the glycine at position 28, all of the amino acids recited by claim 26 are identical to those found in SEQ ID NO: 1. *Id.* According to the Examiner, there is no literal support for a glycine residue at position 28. *Id.*, page 4. The Examiner concludes that claim 26 presents new matter.

Applicants respectfully traverse, but, in order to expedite prosecution, have cancelled claim 26 without prejudice or disclaimer. Applicants have added claims 43-46 to more particularly point out and distinctly claim certain embodiments of their invention. Support for the presence of amino acids other than those found in SEQ ID NO: 1 at positions 28, 43, 48, 111, 125, and 128 is found, for example, in the cDNA sequences SEQ ID NOs: 6 and 7. For example, the protein encoded by SEQ ID NO: 7 has an asparagine at position 28, a methionine at position 43, a glutamine at position 48, an arginine at position 111, a cysteine at position 125, and a phenylalanine at position 128.

The Claims Are Definite

The Examiner also rejected claim 26 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Office Action, page 4. According to the Examiner, the

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

recitation in claim 26 that the claim proteins "comprise" SEQ ID NO: 1 contradicts the recitation in claim 25 that the proteins "consist[ ] essentially of" SEQ ID NO: 1. *Id.*

Without acquiescing in the rejection, Applicants have cancelled claim 26 and added new claim 43, which recites "protein consisting essentially of an amino acid sequence."

The Examiner also contends that claim 26 is indefinite in its recitation of a protein that "'further comprises' specific residues at particular positions of SEQ ID NO: 1." *Id.* According to the Examiner, "it is unclear how SEQ ID NO: 1 can 'further' comprise specific amino acid residues at particular positions of SEQ ID NO: 1 when those residues are already present in SEQ ID NO: 1." *Id.*

Without acquiescing in the rejection, Applicants have cancelled claim 26 and added independent claim 43 rendering this rejection moot.

The Claims Are Not Anticipated

The Examiner rejected claim 25 under 35 U.S.C. § 102(b) as allegedly being anticipated by Stricklin et al., J. Biol. Chem. 258: 12252-12258, 1983 ("Stricklin"). Office Action, page 5. According to the Examiner, Stricklin reports the purification of a collagenase inhibitor from human skin fibroblasts, which comprises the NH_2-terminal 25 amino acids of SEQ ID NO: 1. *Id.* The Examiner cites Carmichael et al., Proc. Natl. Acad. Sci. USA 83: 2407-2411, 1986, as evidence that the protein of SEQ ID NO: 1 is the same as the protein purified by Stricklin. *Id.*

Without acquiescing in the rejection, Applicants have amended claim 25. The proteins encompassed by the amended claim all include NH_2-terminal amino acids in addition to those reported by Stricklin and are not anticipated by that reference.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

Applicants respectfully request withdrawal of the rejection of claim 25 under 35 U.S.C. § 102(b).

Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the application.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: July 1, 2003

By: 
William L. Strauss
Reg. No. 47,114

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

APPENDIX TO AMENDMENT OF JULY 1, 2003

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Amendments to the Specification

Paragraph [016]:

--[016] The coding strand of a first preferred DNA sequence which has been discovered has the following nucleotide sequence (SEQ ID No: 5):

```
        10         20         30         40         50         60
GTTGTTGCTG TGGCTGATAG CCCCAGCAGG GCCTGCACCT GTGTCCCACC CCACCCACAG

        70         80         90        100        110        120
ACGGCCTTCT GCAATTCCGA CCTCGTCATC AGGGCCAAGT TCGTGGGGAC ACCAGAAGTC

       130        140        150        160        170        180
AACCAGACCA CCTTATACCA GCGTTATGAG ATCAAGATGA CCAAGATGTA TAAAGGGTTC

       190        200        210        220        230        240
CAAGCCTTAG GGGATGCCGC TGACATCCGG TTCGTCTACA CCCCCGCCAT GGAGAGTGTC

       250        260        270        280        290        300
TGCGGATACT TCCACAGGTC CCACAACCGC AGCGAGGAGT TTCTCATTGC TGGAAAACTG

       310        320        330        340        350        360
CAGGATGGAC TCTTGCACAT CACTACCTGC AGTTTCGTGG CTCCCTGGAA CAGCCTGAGC

       370        380        390        400        410        420
TTAGCTCAGC GCCGGGGCTT CACCAAGACC TACACTGTTG GCTGTGAGGA ATGCACAGTG

       430        440        450        460        470        480
TTTCCCTGTT TATCCATCCC CTGCAAACTG CAGAGTGGCA CTCATTGCTT GTGGACGGAC

       490        500        510        520        530        540
CAGCTCCTCC AAGGCTCTGA AAAGGGCTTC CAGTCCCGTC ACCTTGCCTG CCTGCCTCGG

       550        560        570        580        590        600
GAGCCAGGGC TGTGCACCTG GCAGTCCCTG CGGTCCCAGA TAGCCTGAAT CCTGCCCGGA

        610        620        630        640        650        660
GTGGAAGCTG AAGCCTGCAC AGTGTCCACC CTGTTCCCAC TCCCATCTTT CTTCCGGACA
```

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

```
       670         680         690         700
ATGAAATAAA GAGTTACCAC CCAGCAAAAA AAAAAAGGAA TTC--
```

Paragraph [018]:

--[018] A second preferred DNA sequence has been discovered which has an additional nucleotide sequence 5' to the initiator sequence. This sequence, which contains as the eighty-second through four-hundred-thirty-second nucleotides nucleotides 1 through 351 of the first preferred sequence set forth above, has the following nucleotide sequence (SEQ ID No: 6):

```
        10          20          30          40          50          60
GGCCATCGCC GCAGATCCAG CGCCCAGAGA GACACCAGAG AACCCACCAT GGCCCCCTTT

        70          80          90         100         110         120
GACCCCTGGC TTCTGCATCC TGTTGTTGCT GTGGCTGATA GCCCCAGCAG GGCCTGCACC

       130         140         150         160         170         180
TGTGTCCCAC CCCACCCACA GACGGCCTTC TGCAATTCCG ACCTCGTCAT CAGGGCCAAG

       190         200         210         220         230         240
TTCGTGGGGA CACCAGAAGT CAACCAGACC ACCTTATACC AGCGTTATGA GATCAAGATG

       250         260         270         280         290         300
ACCAAGATGT ATAAAGGGTT CCAAGCCTTA GGGGATGCCG CTGACATCCG GTTCGTCTAC

       310         320         330         340         350         360
ACCCCCGCCA TGGAGAGTGT CTGCGGATAC TTCCACAGGT CCCACAACCG CAGCGAGGAG

       370         380         390         400         410         420
TTTCTCATTG CTGGAAAACT GCAGGATGGA CTCTTGCACA TCACTACCTG CAGTTTCGTG

       430
GCTCCCTGGA AC--
```

Paragraph [019]:

--[019] A third preferred DNA sequence which incorporates the 5' region of the second preferred sequence and the 3' sequence of the first preferred sequence, has the following nucleotide sequence (SEQ ID No: 7):

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

```
        10          20          30          40          50          60
GGCCATCGCC GCAGATCCAG CGCCCAGAGA GACACCAGAG AACCCACCAT GGCCCCCTTT

        70          80          90         100         110         120
GACCCCTGGC TTCTGCATCC TGTTGTTGCT GTGGCTGATA GCCCCAGCAG GGCCTGCACC

       130         140         150         160         170         180
TGTGTCCCAC CCCACCCACA GACGGCCTTC TGCAATTCCG ACCTCGTCAT CAGGGCCAAG

       190         200         210         220         230         240
TTCGTGGGGA CACCAGAAGT CAACCAGACC ACCTTATACC AGCGTTATGA GATCAAGATG

       250         260         270         280         290         300
ACCAAGATGT ATAAAGGGTT CCAAGCCTTA GGGGATGCCG CTGACATCCG GTTCGTCTAC

       310         320         330         340         350         360
ACCCCCGCCA TGGAGAGTGT CTGCGGATAC TTCCACAGGT CCCACAACCG CAGCGAGGAG

       370         380         390         400         410         420
TTTCTCATTG CTGGAAAACT GCAGGATGGA CTCTTGCACA TCACTACCTG CAGTTTCGTG

       430         440         450         460         470         480
GCTCCCTGGA ACAGCCTGAG CTTAGCTCAG CGCCGGGGCT TCACCAAGAC CTACACTGTT

       490         500         510         520         530         540
GGCTGTGAGG AATGCACAGT GTTTCCCTGT TTATCCATCC CCTGCAAACT GCAGAGTGGC

       550         560         570         580         590         600
ACTCATTGCT TGTGGACGGA CCAGCTCCTC CAAGGCTCTG AAAAGGGCTT CCAGTCCCGT

       610         620         630         640         650         660
CACCTTGCCT GCCTGCCTCG GGAGCCAGGG CTGTGCACCT GGCAGTCCCT GCGGTCCCAG

       670         680         690         700         710         720
ATAGCCTGAA TCCTGCCCGG AGTGGAAGCT GAAGCCTGCA CAGTGTCCAC CCTGTTCCCA

       730         740         750         760         770         780
CTCCCATCTT TCTTCCGGAC AATGAAATAA AGAGTTACCA CCCAGCAAAA AAAAAAAGGA--
```

Paragraph [030]:

--[030] A first preferred portable DNA sequence of the present invention has a nucleotide sequence SEQ ID No: 5 as follows:

```
        10          20          30          40          50          60
GTTGTTGCTG TGGCTGATAG CCCCAGCAGG GCCTGCACCT GTGTCCCACC CCACCCACAG

        70          80          90         100         110         120
ACGGCCTTCT GCAATTCCGA CCTCGTCATC AGGGCCAAGT TCGTGGGGAC ACCAGAAGTC
```

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

```
       130         140         150         160         170         180
AACCAGACCA CCTTATACCA GCGTTATGAG ATCAAGATGA CCAAGATGTA TAAAGGGTTC

       190         200         210         220         230         240
CAAGCCTTAG GGGATGCCGC TGACATCCGG TTCGTCTACA CCCCCGCCAT GGAGAGTGTC

       250         260         270         280         290         300
TGCGGATACT TCCACAGGTC CCACAACCGC AGCGAGGAGT TTCTCATTGC TGGAAAACTG

       310         320         330         340         350         360
CAGGATGGAC TCTTGCACAT CACTACCTGC AGTTTCGTGG CTCCCTGGAA CAGCCTGAGC

       370         380         390         400         410         420
TTAGCTCAGC GCCGGGGCTT CACCAAGACC TACACTGTTG GCTGTGAGGA ATGCACAGTG

       430         440         450         460         470         480
TTTCCCTGTT TATCCATCCC CTGCAAACTG CAGAGTGGCA CTCATTGCTT GTGGACGGAC

       490         500         510         520         530         540
CAGCTCCTCC AAGGCTCTGA AAAGGGCTTC CAGTCCCGTC ACCTTGCCTG CCTGCCTCGG

       550         560         570         580         590         600
GAGCCAGGGC TGTGCACCTG GCAGTCCCTG CGGTCCCAGA TAGCCTGAAT CCTGCCCGGA

        610        620         630         640        650         660
GTGGAAGCTG AAGCCTGCAC AGTGTCCACC CTGTTCCCAC TCCCATCTTT CTTCCGGACA

       670         680         690         700
ATGAAATAAA GAGTTACCAC CCAGCAAAAA AAAAAAGGAA TTC--
```

Paragraph [031]:

--[031] A second preferred portable DNA sequence of the present invention has the following nucleotide sequence (SEQ ID No: 6):

```
        10          20          30          40          50          60
GGCCATCGCC GCAGATCCAG CGCCCAGAGA GACACCAGAG AACCCACCAT GGCCCCCTTT

        70          80          90         100         110         120
GACCCCTGGC TTCTGCATCC TGTTGTTGCT GTGGCTGATA GCCCCAGCAG GGCCTGCACC

       130         140         150         160         170         180
TGTGTCCCAC CCCACCCACA GACGGCCTTC TGCAATTCCG ACCTCGTCAT CAGGGCCAAG

       190         200         210         220         230         240
TTCGTGGGGA CACCAGAAGT CAACCAGACC ACCTTATACC AGCGTTATGA GATCAAGATG

       250         260         270         280         290         300
ACCAAGATGT ATAAAGGGTT CCAAGCCTTA GGGGATGCCG CTGACATCCG GTTCGTCTAC
```

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

```
       310         320         330         340         350         360
ACCCCCGCCA TGGAGAGTGT CTGCGGATAC TTCCACAGGT CCCACAACCG CAGCGAGGAG

       370         380         390         400         410         420
TTTCTCATTG CTGGAAAACT GCAGGATGGA CTCTTGCACA TCACTACCTG CAGTTTCGTG

       430
GCTCCCTGGA AC--
```

Paragraph [033]:

--[033] A third preferred portable DNA sequence has the nucleotide sequence (SEQ ID No: 7):

```
        10          20          30          40          50          60
GGCCATCGCC GCAGATCCAG CGCCCAGAGA GACACCAGAG AACCCACCAT GGCCCCCTTT

        70          80          90         100         110         120
GACCCCTGGC TTCTGCATCC TGTTGTTGCT GTGGCTGATA GCCCCAGCAG GGCCTGCACC

       130         140         150         160         170         180
TGTGTCCCAC CCCACCCACA GACGGCCTTC TGCAATTCCG ACCTCGTCAT CAGGGCCAAG

       190         200         210         220         230         240
TTCGTGGGGA CACCAGAAGT CAACCAGACC ACCTTATACC AGCGTTATGA GATCAAGATG

       250         260         270         280         290         300
ACCAAGATGT ATAAAGGGTT CCAAGCCTTA GGGGATGCCG CTGACATCCG GTTCGTCTAC

       310         320         330         340         350         360
ACCCCCGCCA TGGAGAGTGT CTGCGGATAC TTCCACAGGT CCCACAACCG CAGCGAGGAG

       370         380         390         400         410         420
TTTCTCATTG CTGGAAAACT GCAGGATGGA CTCTTGCACA TCACTACCTG CAGTTTCGTG

       430         440         450         460         470         480
GCTCCCTGGA ACAGCCTGAG CTTAGCTCAG CGCCGGGGCT TCACCAAGAC CTACACTGTT

       490         500         510         520         530         540
GGCTGTGAGG AATGCACAGT GTTTCCCTGT TTATCCATCC CCTGCAAACT GCAGAGTGGC

       550         560         570         580         590         600
ACTCATTGCT TGTGGACGGA CCAGCTCCTC CAAGGCTCTG AAAAGGGCTT CCAGTCCCGT

       610         620         630         640         650         660
CACCTTGCCT GCCTGCCTCG GGAGCCAGGG CTGTGCACCT GGCAGTCCCT GCGGTCCCAG

       670         680         690         700         710         720
ATAGCCTGAA TCCTGCCCGG AGTGGAAGCT GAAGCCTGCA CAGTGTCCAC CCTGTTCCCA
```

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

```
       730         740         750         760         770         780
CTCCCATCTT TCTTCCGGAC AATGAAATAA AGAGTTACCA CCCAGCAAAA AAAAAAAGGA--
```

Paragraph [059]:

--[059] It is anticipated that translation of mRNA coding for the metalloproteinase inhibitor in yeast will be more efficient with the preferred codon usage of yeast than with the sequence present in pUC8-Fic, as identified in Example 2, which has been tailored to the prokaryotic bias. For this reason, the portion of the 5' end of the portable DNA sequence beginning at the *Tth*111I site is preferably resynthesized. The new sequence favors the codons most frequently used in yeast. This new sequence preferably has the following nucleotide sequence:

```
                              HgiAI
(SEQ ID No: 8) 5'  GAT CCG TGC ACT TGT GTT CCA CCA CAC
(SEQ ID No: 9)           GC ACG TGA ACA CAA GGT GGT GTG

                   CCA CAA ACT GCT TTC TGT AAC TCT GAC C
                   GGT GTT TGA CGA AAG ACA TTG AGA CTG GA  3'--
```

Paragraph [075]:

--[075] In this method, the portable DNA sequences are those synthetic or naturally-occurring polynucleotides described above. In a preferred embodiment of the present method, the portable DNA sequence has the nucleotide sequence SEQ ID No: 5 as follows:

```
        10          20          30          40          50          60
GTTGTTGCTG TGGCTGATAG CCCCAGCAGG GCCTGCACCT GTGTCCCACC CCACCCACAG

        70          80          90         100         110         120
ACGGCCTTCT GCAATTCCGA CCTCGTCATC AGGGCCAAGT TCGTGGGGAC ACCAGAAGTC

       130         140         150         160         170         180
AACCAGACCA CCTTATACCA GCGTTATGAG ATCAAGATGA CCAAGATGTA TAAAGGGTTC

       190         200         210         220         230         240
CAAGCCTTAG GGGATGCCGC TGACATCCGG TTCGTCTACA CCCCCGCCAT GGAGAGTGTC
```

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

```
       250         260         270         280         290         300
TGCGGATACT TCCACAGGTC CCACAACCGC AGCGAGGAGT TTCTCATTGC TGGAAAACTG

       310         320         330         340         350         360
CAGGATGGAC TCTTGCACAT CACTACCTGC AGTTTCGTGG CTCCCTGGAA CAGCCTGAGC

       370         380         390         400         410         420
TTAGCTCAGC GCCGGGGCTT CACCAAGACC TACACTGTTG GCTGTGAGGA ATGCACAGTG

       430         440         450         460         470         480
TTTCCCTGTT TATCCATCCC CTGCAAACTG CAGAGTGGCA CTCATTGCTT GTGGACGGAC

       490         500         510         520         530         540
CAGCTCCTCC AAGGCTCTGA AAAGGGCTTC CAGTCCCGTC ACCTTGCCTG CCTGCCTCGG

       550         560         570         580         590         600
GAGCCAGGGC TGTGCACCTG GCAGTCCCTG CGGTCCCAGA TAGCCTGAAT CCTGCCCGGA

        610         620         630         640         650         660
GTGGAAGCTG AAGCCTGCAC AGTGTCCACC CTGTTCCCAC TCCCATCTTT CTTCCGGACA

       670         680         690         700
ATGAAATAAA GAGTTACCAC CCAGCAAAAA AAAAAAGGAA TTC--
```

Paragraph [084]:

--[084] In certain circumstances, the metalloproteinase inhibitor will assume its proper, active structure upon expression in the host microorganism and transport of the protein through the cell wall or membrane into the periplasmic space. This will generally occur if DNA coding for an appropriate leader sequence has been linked to the DNA coding for the recombinant protein. The preferred [metalloprotienase] metalloproteinase inhibitors of the present invention will assume their mature, active form upon translocation out of the inner cell membrane. The structures of numerous signal peptides have been published, for example by Marion E.E. Watson in Nuc. Acid Res. [12: 515-5164] 12: 5145-5164, 1984, specifically incorporated herein by reference. It is intended that these leader sequences, together with portable DNA, will direct intracellular production of a fusion protein which will be transported through the cell

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

membrane and will have the leader sequence portion cleaved upon release from the cell.--

Paragraph [0104]:

--[0104] The structure of FIBAC A is

(SEQ ID No: 10) GA TCC GCG ATC GGA GTG TAA GAA ATG TGC ACT
(SEQ ID No: 11) G CGC TAG CCT CAC ATT CTT TAC ACG TGA

TGC GTT CCG CCG CAT CCG CAG ACT GCT TTC
ACG CAA GGC GGC GTA GGC GTC TGA CGA AAG

TGC AAC TCT GAC C
ACG TTG AGA CTG GA--

Paragraph [0106]:

--[0106] Component oligonucleotide FA1 (SEQ ID No: 12) is:
GATCC GCGAT CGGAG TGTAA GAAAT GTGCA CTTGC--

Paragraph [0107]:

--[0107] Component oligonucleotide FA2 (SEQ ID No: 13) is:
GGAACG CAAGT GCACA TTTCT TACAC TCCGA TCGCG--

Paragraph [0108]:

--[0108] Component oligonucleotide FA3 (SEQ ID No: 14) is:
GTTC CGCCG CATCC GCAGA CTGCT TTCTG CAACT CTGAC C--

Paragraph [0109]:

--[0109] Component oligonucleotide FA4 (SEQ ID No: 15) is:
AGGTC AGAGT TGCAG AAAGC AGTCT GCGGA TGCGG C--

Paragraph [0112]:

--[0112] Linker A1 (SEQ ID No: 16) is: AATTGGCAG--

Paragraph [0113]:

--[0113] Linker A2 (SEQ ID No: 17) is: TCGACTGCC--

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

Paragraph [0116]:

--[0116] The sequence of the sense strand (SEQ ID No: 18) is:

```
         10          20          30          40          50          60
GAATTCGATA TCTCGTTGGA GATATTCATG ACGTATTTTG GATGATAACG AGGCGCAAAA
E    T E                                    F           M   H
C    A C                                    O           N   H
O    Q O                                    K           L   A
1    1 5                                    1           1   1

         70          80          90         100        110
AATGAAAAAG ACAGCTATCG CGATCGCAGT GGCACTGGCT GGTTTCGCTA CCGTA
              A     NF  PS
              L     RN  VA
              U     UU  UU
              1     12  1A

  120         130
GCGCA GGCCTCTGGT AAAAGCTT
H    S H M           HA
H    T A N           IL
A    U E L            NU
1    1 3 1           31--
```

Paragraph [0120]:

--[0120] Linker B1 (SEQ ID No: 19) is: GATCCCAGGCCTGCA--

Paragraph [0121]:

--[0121] Linker B2 (SEQ ID No: 20) is: GGCCTGG--

Paragraph [0136]:

--[0136] The second preferred sequence (SEQ ID No: 6) as set forth herein, i.e.,

```
         10          20          30          40          50          60
GGCCATCGCC GCAGATCCAG CGCCCAGAGA GACACCAGAG AACCCACCAT GGCCCCCTTT

         70          80          90         100         110         120
GACCCCTGGC TTCTGCATCC TGTTGTTGCT GTGGCTGATA GCCCCAGCAG GGCCTGCACC

        130         140         150         160         170         180
TGTGTCCCAC CCCACCCACA GACGGCCTTC TGCAATTCCG ACCTCGTCAT CAGGGCCAAG

        190         200         210         220         230         240
TTCGTGGGGA CACCAGAAGT CAACCAGACC ACCTTATACC AGCGTTATGA GATCAAGATG

        250         260         270         280         290         300
```

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

```
ACCAAGATGT ATAAAGGGTT CCAAGCCTTA GGGGATGCCG CTGACATCCG GTTCGTCTAC

       310        320        330        340        350        360
ACCCCCGCCA TGGAGAGTGT CTGCGGATAC TTCCACAGGT CCCACAACCG CAGCGAGGAG

       370        380        390        400        410        420
TTTCTCATTG CTGGAAAACT GCAGGATGGA CTCTTGCACA TCACTACCTG CAGTTTCGTG

       430
GCTCCCTGGA AC--
```

Amendments to the Claims:

Claim 25:

25. (Amended) A purified collagenase inhibitor protein, said protein consisting essentially of an amino acid sequence selected from among the following:

[a) amino acid sequence SEQ ID NO: 1; or]

[b]a) amino acid sequence SEQ ID NO: 2; or

[c]b) the amino acid sequence[s] of a) or of SEQ ID NO: 1 [b)], further having a Met at position -1; or

[d]c) the amino acid sequence of a) or of SEQ ID NO: 1 [b)], further having a leader sequence at the N-terminal, -1 position, wherein said leader sequence consists essentially of the following amino acid sequence from positions -38 to -1:

Gly His Arg Arg Arg Ser Ser Ala Gln Arg Asp Thr Arg Glu Pro Thr Met Ala Pro Phe Asp Pro Trp Leu Leu His Pro Val Val Ala Val Ala Asp Ser Pro Ser Arg Ala (SEQ ID NO: 3); or

[e]d) the amino acid sequence of a) or of SEQ ID NO: 1, [b)] further having a leader sequence at the N-terminal, -1 position, wherein said leader sequence consists essentially of the following amino acid sequence from positions -22 to -1: Met Ala Pro Phe Asp Pro Trp Leu Leu His Pro Val Val Ala Val Ala Asp Ser Pro Ser Arg Ala (SEQ ID NO: 4).

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com